

SEQUENCE LISTING

<110> Garvan Institute of Medical Research

<120> Methods of validating target for modulating insulin action, screening for modulators of insulin action and therapeutic uses thereof

<130> 502965/MRO

<150> AU 2003906285

<151> 2003-11-14

<150> AU 2003906286

<151> 2002-11-14

<160> 268

<170> PatentIn version 3.1

<210> 1

<211> 153

<212> PRT

<213> disrupted mouse Cbl

<400> 1

Met Ala Gly Asn Val Lys Lys Ser Ser Gly Ala Gly Gly Gly Gly Ser
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Gly Gly Ser Gly Ala Gly Gly Leu Ile Gly Leu Met Lys Asp Ala Phe
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Gln Pro His His His His His His Leu Ser Pro His Pro Pro Cys Thr
35 40 45

Val Asp Lys Lys Met Val Glu Lys Cys Trp Lys Leu Met Asp Lys Val
50 55 60

Val Arg Leu Cys Gln Asn Pro Asn Val Ala Leu Lys Asn Ser Pro Pro
65 70 75 80

Tyr Ile Leu Asp Leu Leu Pro Asp Thr Tyr Gln His Leu Arg Thr Val
85 90 95

Leu Ser Arg Tyr Glu Gly Lys Met Glu Thr Leu Gly Glu Asn Glu Tyr
100 105 110

Phe Arg Val Phe Met Glu Asn Leu Met Lys Lys Thr Lys Gln Thr Ile
115 120 125

Ser Leu Phe Lys Glu Gly Lys Glu Arg Met Tyr Glu Glu Asn Ser Gln
130 135 140

Pro Arg Arg Asn Leu Thr Lys Leu Ser
145 150

<210> 2

<211> 896

<212> PRT

<213> native full-length mouse Cbl

<400> 2

Met Ala Gly Asn Val Lys Lys Ser Ser Gly Ala Gly Gly Gly Gly Ser
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Gly Gly Ser Gly Ala Gly Gly Leu Ile Gly Leu Met Lys Asp Ala Phe
 20 25 30

Gln Pro His His His His His Leu Ser Pro His Pro Pro Cys Thr
 35 40 45

Val Asp Lys Lys Met Val Glu Lys Cys Trp Lys Leu Met Asp Lys Val
 50 55 60

Val Arg Leu Cys Gln Asn Pro Asn Val Ala Leu Lys Asn Ser Pro Pro
 65 70 75 80

Tyr Ile Leu Asp Leu Leu Pro Asp Thr Tyr Gln His Leu Arg Thr Val
 85 90 95

Leu Ser Arg Tyr Glu Gly Lys Met Glu Thr Leu Gly Glu Asn Glu Tyr
 100 105 110

Phe Arg Val Phe Met Glu Asn Leu Met Lys Lys Thr Lys Gln Thr Ile
 115 120 125

Ser Leu Phe Lys Glu Gly Lys Glu Arg Met Tyr Glu Glu Asn Ser Gln
 130 135 140

Pro Arg Arg Asn Leu Thr Lys Leu Ser Leu Ile Phe Ser His Met Leu
 145 150 155 160

Ala Glu Leu Lys Gly Ile Phe Pro Ser Gly Leu Phe Gln Gly Asp Thr
 165 170 175

Phe Arg Ile Thr Lys Ala Asp Ala Ala Glu Phe Trp Arg Lys Ala Phe
 180 185 190

Gly Glu Lys Thr Ile Val Pro Trp Lys Ser Phe Arg Gln Ala Leu His
 195 200 205

Glu Val His Pro Ile Ser Ser Gly Leu Glu Ala Met Ala Leu Lys Ser
 210 215 220

Thr Ile Asp Leu Thr Cys Asn Asp Tyr Ile Ser Val Phe Glu Phe Asp
 225 230 235 240

Ile Phe Thr Arg Leu Phe Gln Pro Trp Ser Ser Leu Leu Arg Asn Trp
 245 250 255

Asn Ser Leu Ala Val Thr His Pro Gly Tyr Met Ala Phe Leu Thr Tyr
 260 265 270

Asp Glu Val Lys Ala Arg Leu Gln Lys Phe Ile His Lys Pro Gly Ser
 275 280 285

Tyr Ile Phe Arg Leu Ser Cys Thr Arg Leu Gly Gln Trp Ala Ile Gly
 290 295 300

Tyr Val Thr Ala Asp Gly Asn Ile Leu Gln Thr Ile Pro His Asn Lys
 305 310 315 320

Pro Leu Phe Gln Ala Leu Ile Asp Gly Phe Arg Glu Gly Phe Tyr Leu
 325 330 335

Phe Pro Asp Gly Arg Asn Gln Asn Pro Asp Leu Thr Gly Leu Cys Glu
 340 345 350

Pro Thr Pro Gln Asp His Ile Lys Val Thr Gln Ile Cys Ala Glu Asn
 355 360 365

Asp Lys Asp Val Lys Ile Glu Pro Cys Gly His Leu Met Cys Thr Ser
 370 375 380

Cys Leu Thr Ser Trp Gln Glu Ser Glu Gly Gln Gly Cys Pro Phe Cys
 385 390 395 400

Arg Cys Glu Ile Lys Gly Thr Glu Pro Ile Val Val Asp Pro Phe Asp
 405 410 415

Pro Arg Gly Ser Gly Ser Leu Leu Arg Gln Gly Ala Glu Gly Ala Pro
 420 425 430

Ser Pro Asn Tyr Asp Asp Asp Asp Asp Glu Arg Ala Asp Asp Ser Leu
 435 440 445

Phe Met Met Lys Glu Leu Ala Gly Ala Lys Val Glu Arg Pro Ser Ser
 450 455 460

Pro Phe Ser Met Ala Pro Gln Ala Ser Leu Pro Pro Val Pro Pro Arg
 465 470 475 480

Leu Asp Leu Leu Gln Gln Arg Ala Pro Val Pro Ala Ser Thr Ser Val
 485 490 495

Leu Gly Thr Ala Ser Lys Ala Ala Ser Gly Ser Leu His Lys Asp Lys
 500 505 510

Pro Leu Pro Ile Pro Pro Thr Leu Arg Asp Leu Pro Pro Pro Pro Pro
515 520 525

Pro Asp Arg Pro Tyr Ser Val Gly Ala Glu Thr Arg Pro Gln Arg Arg
530 535 540

Pro Leu Pro Cys Thr Pro Gly Asp Cys Pro Ser Arg Asp Lys Leu Pro
545 550 555 560

Pro Val Pro Ser Ser Arg Pro Gly Asp Ser Trp Leu Ser Arg Thr Ile
565 570 575

Pro Lys Val Pro Val Ala Thr Pro Asn Pro Gly Asp Pro Trp Asn Gly
580 585 590

Arg Glu Leu Thr Asn Arg His Ser Leu Pro Phe Ser Leu Pro Ser Gln
595 600 605

Met Glu Pro Arg Ala Asp Val Pro Arg Leu Gly Ser Thr Phe Ser Leu
610 615 620

Asp Thr Ser Met Thr Met Asn Ser Ser Pro Val Ala Gly Pro Glu Ser
625 630 635 640

Glu His Pro Lys Ile Lys Pro Ser Ser Ser Ala Asn Ala Ile Tyr Ser
645 650 655

Leu Ala Ala Arg Pro Leu Pro Met Pro Lys Leu Pro Pro Gly Glu Gln
660 665 670

Gly Glu Ser Glu Glu Asp Thr Glu Tyr Met Thr Pro Thr Ser Arg Pro
675 680 685

Val Gly Val Gln Lys Pro Glu Pro Lys Arg Pro Leu Glu Ala Thr Gln
690 695 700

Ser Ser Arg Ala Cys Asp Cys Asp Gln Gln Ile Asp Ser Cys Thr Tyr
705 710 715 720

Glu Ala Met Tyr Thr Ile Gln Ser Gln Ala Leu Ser Val Ala Glu Asn
725 730 735

Ser Ala Ser Gly Glu Gly Asn Leu Ala Thr Ala His Thr Ser Thr Gly
740 745 750

Pro Glu Glu Ser Glu Asn Glu Asp Asp Gly Tyr Asp Val Pro Lys Pro
755 760 765

Pro Val Pro Ala Val Leu Ala Arg Arg Thr Leu Ser Asp Ile Ser Asn
770 775 780

Ala Ser Ser Ser Phe Gly Trp Leu Ser Leu Asp Gly Asp Pro Thr Asn
 785 790 795 800

Phe Asn Glu Gly Ser Gln Val Pro Glu Arg Pro Pro Lys Pro Phe Pro
 805 810 815

Arg Arg Ile Asn Ser Glu Arg Lys Ala Ser Ser Tyr Gln Gln Gly Gly
 820 825 830

Gly Ala Thr Ala Asn Pro Val Ala Thr Ala Pro Ser Pro Gln Leu Ser
 835 840 845

Ser Glu Ile Glu Arg Leu Met Ser Gln Gly Tyr Ser Tyr Gln Asp Ile
 850 855 860

Gln Lys Ala Leu Val Ile Ala His Asn Asn Ile Glu Met Ala Lys Asn
 865 870 875 880

Ile Leu Arg Glu Phe Val Ser Ile Ser Ser Pro Ala His Val Ala Thr
 885 890 895

<210> 3

<211> 906

<212> PRT

<213> native full-length human c-Cbl

<400> 3

Met Ala Gly Asn Val Lys Lys Ser Ser Gly Ala Gly Gly Gly Thr Gly
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Ser Gly Gly Ser Gly Ser Gly Gly Leu Ile Gly Leu Met Lys Asp Ala
 20 25 30

Phe Gln Pro His His His His His His His Leu Ser Pro His Pro Pro
 35 40 45

Gly Thr Val Asp Lys Lys Met Val Glu Lys Cys Trp Lys Leu Met Asp
 50 55 60

Lys Val Val Arg Leu Cys Gln Asn Pro Lys Leu Ala Leu Lys Asn Ser
 65 70 75 80

Pro Pro Tyr Ile Leu Asp Leu Leu Pro Asp Thr Tyr Gln His Leu Arg
 85 90 95

Thr Ile Leu Ser Arg Tyr Glu Gly Lys Met Glu Thr Leu Gly Glu Asn
 100 105 110

Glu Tyr Phe Arg Val Phe Met Glu Asn Leu Met Lys Lys Thr Lys Gln
115 120 125

Thr Ile Ser Leu Phe Lys Glu Gly Lys Glu Arg Met Tyr Glu Glu Asn
130 135 140

Ser Gln Pro Arg Arg Asn Leu Thr Lys Leu Ser Leu Ile Phe Ser His
145 150 155 160

Met Leu Ala Glu Leu Lys Gly Ile Phe Pro Ser Gly Leu Phe Gln Gly
165 170 175

Asp Thr Phe Arg Ile Thr Lys Ala Asp Ala Ala Glu Phe Trp Arg Lys
180 185 190

Ala Phe Gly Glu Lys Thr Ile Val Pro Trp Lys Ser Phe Arg Gln Ala
195 200 205

Leu His Glu Val His Pro Ile Ser Ser Gly Leu Glu Ala Met Ala Leu
210 215 220

Lys Ser Thr Ile Asp Leu Thr Cys Asn Asp Tyr Ile Ser Val Phe Glu
225 230 235 240

Phe Asp Ile Phe Thr Arg Leu Phe Gln Pro Trp Ser Ser Leu Leu Arg
245 250 255

Asn Trp Asn Ser Leu Ala Val Thr His Pro Gly Tyr Met Ala Phe Leu
260 265 270

Thr Tyr Asp Glu Val Lys Ala Arg Leu Gln Lys Phe Ile His Lys Pro
275 280 285

Gly Ser Tyr Ile Phe Arg Leu Ser Cys Thr Arg Leu Gly Gln Trp Ala
290 295 300

Ile Gly Tyr Val Thr Ala Asp Gly Asn Ile Leu Gln Thr Ile Pro His
305 310 315 320

Asn Lys Pro Leu Phe Gln Ala Leu Ile Asp Gly Phe Arg Glu Gly Phe
325 330 335

Tyr Leu Phe Pro Asp Gly Arg Asn Gln Asn Pro Asp Leu Thr Gly Leu
340 345 350

Cys Glu Pro Thr Pro Gln Asp His Ile Lys Val Thr Gln Glu Gln Tyr
355 360 365

Glu Leu Tyr Cys Glu Met Gly Ser Thr Phe Gln Leu Cys Lys Ile Cys
370 375 380

Ala Glu Asn Asp Lys Asp Val Lys Ile Glu Pro Cys Gly His Leu Met
385 390 395 400

Cys Thr Ser Cys Leu Thr Ser Trp Gln Glu Ser Glu Gly Gln Gly Cys
405 410 415

Pro Phe Cys Arg Cys Glu Ile Lys Gly Thr Glu Pro Ile Val Val Asp
420 425 430

Pro Phe Asp Pro Arg Gly Ser Gly Ser Leu Leu Arg Gln Gly Ala Glu
435 440 445

Gly Ala Pro Ser Pro Asn Tyr Asp Asp Asp Asp Asp Glu Arg Ala Asp
450 455 460

Asp Thr Leu Phe Met Met Lys Glu Leu Ala Gly Ala Lys Val Glu Arg
465 470 475 480

Pro Pro Ser Pro Phe Ser Met Ala Pro Gln Ala Ser Leu Pro Pro Val
485 490 495

Pro Pro Arg Leu Asp Leu Leu Pro Gln Arg Val Cys Val Pro Ser Ser
500 505 510

Ala Ser Ala Leu Gly Thr Ala Ser Lys Ala Ala Ser Gly Ser Leu His
515 520 525

Lys Asp Lys Pro Leu Pro Val Pro Pro Thr Leu Arg Asp Leu Pro Pro
530 535 540

Pro Pro Pro Pro Asp Arg Pro Tyr Ser Val Gly Ala Glu Ser Arg Pro
545 550 555 560

Gln Arg Arg Pro Leu Pro Cys Thr Pro Gly Asp Cys Pro Ser Arg Asp
565 570 575

Lys Leu Pro Pro Val Pro Ser Ser Arg Leu Gly Asp Ser Trp Leu Pro
580 585 590

Arg Pro Ile Pro Lys Val Pro Val Ser Ala Pro Ser Ser Ser Asp Pro
595 600 605

Trp Thr Gly Arg Glu Leu Thr Asn Arg His Ser Leu Pro Phe Ser Leu
610 615 620

Pro Ser Gln Met Glu Pro Arg Pro Asp Val Pro Arg Leu Gly Ser Thr
625 630 635 640

Phe Ser Leu Asp Thr Ser Met Ser Met Asn Ser Ser Pro Leu Val Gly
645 650 655

Pro Glu Cys Asp His Pro Lys Ile Lys Pro Ser Ser Ser Ala Asn Ala
660 665 670

Ile Tyr Ser Leu Ala Ala Arg Pro Leu Pro Val Pro Lys Leu Pro Pro
675 680 685

Gly Glu Gln Cys Glu Gly Glu Glu Asp Thr Glu Tyr Met Thr Pro Ser
690 695 700

Ser Arg Pro Leu Arg Pro Leu Asp Thr Ser Gln Ser Ser Arg Ala Cys
705 710 715 720

Asp Cys Asp Gln Gln Ile Asp Ser Cys Thr Tyr Glu Ala Met Tyr Asn
725 730 735

Ile Gln Ser Gln Ala Pro Ser Ile Thr Glu Ser Ser Thr Phe Gly Glu
740 745 750

Gly Asn Leu Ala Ala Ala His Ala Asn Thr Gly Pro Glu Glu Ser Glu
755 760 765

Asn Glu Asp Asp Gly Tyr Asp Val Pro Lys Pro Pro Val Pro Ala Val
770 775 780

Leu Ala Arg Arg Thr Leu Ser Asp Ile Ser Asn Ala Ser Ser Ser Phe
785 790 795 800

Gly Trp Leu Ser Leu Asp Gly Asp Pro Thr Thr Asn Val Thr Glu Gly
805 810 815

Ser Gln Val Pro Glu Arg Pro Pro Lys Pro Phe Pro Arg Arg Ile Asn
820 825 830

Ser Glu Arg Lys Ala Gly Ser Cys Gln Gln Gly Ser Gly Pro Ala Ala
835 840 845

Ser Ala Ala Thr Ala Ser Pro Gln Leu Ser Ser Glu Ile Glu Asn Leu
850 855 860

Met Ser Gln Gly Tyr Ser Tyr Gln Asp Ile Gln Lys Ala Leu Val Ile
865 870 875 880

Ala Gln Asn Asn Ile Glu Met Ala Lys Asn Ile Leu Arg Glu Phe Val
885 890 895

Ser Ile Ser Ser Pro Ala His Val Ala Thr
900 905

<211> 2483

<212> PRT

<213> homosapiens Acteyl CoA carboxylase (ACC2)

<400> 4

Met Val Leu Leu Leu Cys Leu Ser Cys Leu Ile Phe Ser Cys Leu Thr
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Phe Ser Trp Leu Lys Ile Trp Glu Lys Met Thr Asp Ser Lys Pro Ile
 20 25 30

Thr Lys Ser Lys Ser Glu Ala Asn Leu Ile Pro Ser Gln Glu Pro Phe
 35 40 45

Pro Ala Ser Asp Asn Ser Gly Glu Thr Pro Gln Arg Asn Gly Glu Gly
 50 55 60

His Thr Leu His Lys Asp Thr Gln Pro Gly Arg Ala Gln Pro Pro Thr
 65 70 75 80

Lys Ala Gln Arg Ser Gly Arg Arg Arg Asn Ser Leu Pro Pro Ser Arg
 85 90 95

Gln Lys Pro Pro Arg Asn Pro Leu Ser Ser Ser Asp Ala Ala Pro Ser
 100 105 110

Pro Glu Leu Gln Ala Asn Gly Thr Gly Thr Gln Gly Leu Glu Ala Thr
 115 120 125

Asp Thr Asn Gly Leu Ser Ser Ser Ala Arg Pro Gln Gly Ser Lys Leu
 130 135 140

Val Pro Ser Lys Glu Asp Lys Lys Gln Ala Asn Ile Lys Arg Gln Leu
 145 150 155 160

Met Thr Asn Phe Ile Leu Gly Ser Phe Asp Asp Tyr Ser Ser Asp Glu
 165 170 175

Asp Ser Val Ala Gly Ser Ser Arg Glu Ser Thr Arg Lys Gly Ser Arg
 180 185 190

Ala Ser Leu Gly Ala Leu Ser Leu Glu Ala Tyr Leu Thr Thr Gly Glu
 195 200 205

Ala Glu Thr Arg Val Pro Thr Met Arg Pro Ser Met Ser Gly Leu His
 210 215 220

Leu Val Lys Arg Gly Arg Glu His Lys Lys Leu Asp Leu His Arg Asp
 225 230 235 240

Phe Thr Val Ala Ser Pro Ala Glu Phe Val Thr Arg Phe Gly Gly Asp
 245 250 255

Arg Val Ile Glu Lys Val Leu Ile Ala Asn Asn Gly Ile Ala Ala Val
 260 265 270

Lys Cys Met Arg Ser Ile Arg Arg Trp Ala Tyr Glu Met Phe Arg Asn
 275 280 285

Glu Arg Ala Ile Arg Phe Val Arg Met Val Thr Pro Glu Asp Leu Lys
 290 295 300

Ala Asn Ala Glu Tyr Ile Lys Met Ala Asp His Tyr Gly Pro Ala Pro
 305 310 315 320

Gly Gly Pro Asn Asn Asn Asn Tyr Ala Asn Val Glu Leu Ile Val Asp
 325 330 335

Ile Ala Lys Arg Ile Pro Leu Gln Ala Val Trp Ala Gly Trp Gly His
 340 345 350

Ala Leu Glu Asn Pro Lys Leu Pro Glu Leu Leu Cys Lys Asn Gly Val
 355 360 365

Ala Phe Leu Gly Pro Pro Arg Leu Arg Pro Met Val Gly Leu Gly Asp
 370 375 380

Lys Ile Ala Ser Thr Val Val Ala Gln Thr Leu Gln Val Pro Thr Leu
 385 390 395 400

Pro Arg Ser Gly Ser Ala Leu Thr Val Glu Trp Thr Glu Asp Asp Leu
 405 410 415

Gln Gln Gly Lys Arg Ile Ser Val Pro Glu Asp Val Tyr Asp Lys Gly
 420 425 430

Cys Val Lys Asp Val Asp Glu Gly Leu Glu Ala Ala Glu Arg Ile Gly
 435 440 445

Phe Pro Leu Met Ile Lys Ala Ser Glu Gly Gly Gly Gly Lys Gly Ile
 450 455 460

Arg Glu Thr Glu Ser Ala Glu Asp Phe Pro Ile Leu Phe Arg Gln Val
 465 470 475 480

Gln Ser Glu Ile Pro Gly Ser Pro Ile Phe Leu Met Lys Leu Ala Gln
 485 490 495

His Ala Arg His Leu Glu Val Gln Ile Leu Ala Asp Gln Tyr Gly Asn
 500 505 510

Ala Val Ser Leu Phe Gly Arg Asp Cys Ser Ile Gln Arg Arg His Gln
515 520 525

Lys Ile Val Glu Glu Ala Pro Ala Thr Ile Ala Pro Leu Ala Ile Phe
530 535 540

Glu Phe Met Glu Gln Cys Ala Ile Arg Leu Ala Lys Thr Val Gly Tyr
545 550 555 560

Val Ser Ala Gly Thr Val Glu Tyr Leu Tyr Ser Gln Asp Gly Ser Phe
565 570 575

His Phe Leu Glu Leu Asn Pro Arg Leu Gln Val Glu His Pro Cys Thr
580 585 590

Glu Met Ile Ala Asp Val Asn Leu Pro Ala Ala Gln Leu Gln Ile Ala
595 600 605

Met Gly Ala Pro Leu His Arg Leu Lys Asp Ile Arg Leu Leu Tyr Gly
610 615 620

Glu Ser Pro Trp Gly Asp Ser Pro Ile Ser Phe Glu Asn Ser Ala His
625 630 635 640

Leu Pro Cys Pro Arg Gly His Val Ile Ala Thr Arg Ile Thr Ser Glu
645 650 655

Asn Pro Asp Glu Gly Phe Lys Pro Ser Ser Gly Thr Val Gln Glu Leu
660 665 670

Asn Phe Arg Ser Ser Lys Asn Val Trp Gly Tyr Phe Thr Val Ala Ala
675 680 685

Thr Gly Gly Leu His Glu Phe Ala Ile Ser Gln Phe Gly His Cys Phe
690 695 700

Ser Trp Gly Glu Asn Arg Lys Glu Ala Ile Ser Asn Met Val Val Ala
705 710 715 720

Leu Lys Glu Leu Ser Leu Arg Gly Asp Phe Arg Thr Thr Val Glu Tyr
725 730 735

Leu Ile Asn Leu Leu Glu Thr Glu Ser Phe Gln Asn Asn Tyr Ile Asp
740 745 750

Thr Gly Trp Leu Asp Tyr Leu Ile Ala Glu Lys Val Gln Lys Lys Pro
755 760 765

Asn Ile Met Leu Gly Val Val Cys Gly Ala Leu Glu Arg Gly Asp Ala
770 775 780

Met Phe Arg Thr Cys Met Thr Asp Phe Leu His Ser Leu Glu Arg Gly
 785 790 795 800
 Gln Val Leu Pro Ala Asp Ser Leu Leu Asn Leu Val Asp Val Glu Leu
 805 810 815
 Ile Tyr Glu Gly Val Lys Tyr Ile Leu Lys Val Thr Arg Gln Ser Leu
 820 825 830
 Thr Met Phe Val Leu Ile Met Asn Gly Cys His Ile Glu Ile Asp Ala
 835 840 845
 His Arg Leu Asn Asp Gly Gly Leu Leu Leu Ser Tyr Asn Gly Asn Ser
 850 855 860
 Tyr Thr Thr Tyr Met Lys Glu Glu Val Asp Ser Tyr Arg Thr Ile Gly
 865 870 875 880
 Asn Lys Thr Cys Val Phe Glu Lys Glu Asn Asp Pro Thr Val Leu Arg
 885 890 895
 Ser Pro Ser Ala Gly Lys Leu Thr Gln Ile Thr Val Glu Asp Gly Gly
 900 905 910
 His Val Glu Ala Gly Arg Arg Tyr Ala Glu Met Glu Val Met Lys Met
 915 920 925
 Ile Met Thr Leu Asn Val Gln Glu Arg Gly Arg Val Lys Tyr Ile Lys
 930 935 940
 Arg Pro Gly Ala Val Leu Glu Ala Gly Cys Val Val Ala Arg Leu Glu
 945 950 955 960
 Leu Asp Asp Pro Ser Lys Val His Pro Ala Glu Pro Phe Thr Gly Glu
 965 970 975
 Leu Pro Ala Gln Gln Asn Thr Ala Asp Leu Gly Lys Lys Leu His Arg
 980 985 990
 Val Phe His Ser Val Leu Gly Ser Leu Thr Asn Val Met Ser Gly Phe
 995 1000 1005
 Cys Leu Pro Glu Pro Phe Phe Ser Ile Lys Leu Lys Glu Trp Val
 1010 1015 1020
 Gln Lys Leu Met Met Thr Leu Arg His Pro Ser Leu Leu Leu Asp
 1025 1030 1035
 Val Gln Glu Ile Met Thr Ser Arg Ala Gly Arg Ile Pro Pro Pro
 1040 1045 1050

Val	Glu	Lys	Ser	Val	Arg	Lys	Val	Met	Ala	Gln	Tyr	Ala	Ser	Asn
1055						1060					1065			
Ile	Thr	Ser	Val	Leu	Cys	Gln	Phe	Pro	Ser	Gln	Gln	Ile	Ala	Thr
1070						1075					1080			
Ile	Leu	Asp	Cys	His	Ala	Ala	Thr	Leu	Gln	Arg	Lys	Ala	Asp	Arg
1085						1090					1095			
Glu	Val	Phe	Phe	Ile	Asn	Thr	Gln	Ser	Met	Val	Gln	Leu	Val	Gln
1100						1105					1110			
Arg	Tyr	Arg	Ser	Gly	Ile	Arg	Gly	His	Met	Lys	Thr	Val	Val	Ile
1115						1120					1125			
Asp	Leu	Leu	Arg	Arg	Tyr	Leu	Arg	Val	Glu	Thr	Ile	Phe	Gly	Lys
1130						1135					1140			
Ala	Arg	Asp	Ala	Asp	Ala	Asn	Ser	Ser	Gly	Met	Val	Gly	Gly	Val
1145						1150					1155			
Arg	Ser	Leu	Ser	Phe	Thr	Ser	Val	Trp	Val	Val	Leu	Ser	Pro	Pro
1160						1165					1170			
Ala	His	Tyr	Asp	Lys	Cys	Val	Ile	Asn	Leu	Arg	Glu	Gln	Phe	Lys
1175						1180					1185			
Pro	Asp	Met	Ser	Gln	Val	Leu	Asp	Cys	Ile	Phe	Ser	His	Ala	Gln
1190						1195					1200			
Val	Thr	Lys	Lys	Asn	Gln	Leu	Val	Ile	Met	Leu	Ile	Asp	Glu	Leu
1205						1210					1215			
Cys	Gly	Pro	Asp	Pro	Ser	Leu	Ser	Asp	Glu	Leu	Ile	Ser	Ile	Leu
1220						1225					1230			
Asn	Glu	Leu	Thr	Gln	Leu	Ser	Lys	Ser	Glu	His	Cys	Lys	Val	Ala
1235						1240					1245			
Leu	Arg	Ala	Arg	Gln	Ile	Leu	Ile	Ala	Ser	Pro	Ser	Tyr	Glu	Leu
1250						1255					1260			
Arg	His	Asn	Gln	Val	Glu	Ser	Ile	Phe	Leu	Ser	Ala	Ile	Asp	Met
1265						1270					1275			
Tyr	Gly	His	Gln	Phe	Cys	Pro	Glu	Asn	Leu	Gln	Lys	Leu	Ile	Leu
1280						1285					1290			
Ser	Glu	Thr	Thr	Ile	Phe	Asp	Val	Leu	Asn	Thr	Phe	Phe	Tyr	His
1295						1300					1305			

Ala	Asn	Lys	Val	Val	Cys	Met	Ala	Ser	Leu	Glu	Val	Tyr	Val	Gly
1310						1315					1320			
Gly	Ala	Tyr	Ile	Ala	Tyr	Val	Leu	Asn	Ser	Leu	Gln	His	Arg	Gln
1325						1330					1335			
Leu	Pro	Asp	Gly	Thr	Cys	Val	Val	Glu	Phe	Gln	Phe	Met	Leu	Pro
1340						1345					1350			
Ser	Ser	His	Pro	Asn	Arg	Met	Thr	Val	Pro	Ile	Ser	Ile	Thr	Asn
1355						1360					1365			
Pro	Asp	Leu	Leu	Arg	His	Thr	Thr	Glu	Leu	Phe	Met	Asp	Ser	Gly
1370						1375					1380			
Phe	Ser	Pro	Leu	Cys	Gln	Arg	Met	Gly	Ala	Met	Val	Ala	Phe	Arg
1385						1390					1395			
Arg	Phe	Glu	Asp	Phe	Thr	Arg	Asn	Phe	Asp	Glu	Val	Ile	Ser	Cys
1400						1405					1410			
Phe	Ala	Asn	Val	Pro	Lys	Asp	Pro	Pro	Leu	Phe	Ser	Glu	Ala	Arg
1415						1420					1425			
Thr	Ser	Leu	Tyr	Ser	Glu	Asp	Asp	Cys	Lys	Ser	Leu	Arg	Glu	Glu
1430						1435					1440			
Pro	Ile	His	Ile	Leu	Asn	Val	Ser	Ile	Gln	Cys	Ala	Asp	His	Leu
1445						1450					1455			
Glu	Asp	Glu	Ala	Leu	Val	Pro	Ile	Leu	Arg	Thr	Phe	Val	Gln	Ser
1460						1465					1470			
Lys	Lys	Asn	Ile	Leu	Val	Asp	Tyr	Gly	Leu	Arg	Arg	Ile	Pro	Phe
1475						1480					1485			
Leu	Ile	Ala	Gln	Glu	Lys	Glu	Phe	Pro	Lys	Phe	Phe	Thr	Phe	Arg
1490						1495					1500			
Ala	Arg	Asp	Glu	Phe	Ala	Glu	Asp	Arg	Ile	Tyr	Arg	His	Leu	Glu
1505						1510					1515			
Pro	Ala	Leu	Ala	Phe	Gln	Leu	Glu	Leu	Asn	Arg	Met	Arg	Asn	Phe
1520						1525					1530			
Asp	Leu	Thr	Ala	Val	Pro	Cys	Ala	Asn	His	Lys	Met	His	Leu	Tyr
1535						1540					1545			
Leu	Gly	Ala	Ala	Lys	Val	Glu	Gly	Arg	Tyr	Glu	Val	Thr	Asp	His
1550						1555					1560			

Arg Phe	Phe Ile	Arg Ala	Ile	Ile Arg	His Ser	Asp	Leu Ile	Thr	
1565			1570			1575			
Lys Glu	Ala Ser	Phe Glu	Tyr	Leu Gln	Asn Glu	Gly	Glu Arg	Leu	
1580			1585			1590			
Leu Leu	Glu Ala	Met Asp	Glu	Leu Glu	Val Ala	Phe	Asn Asn	Thr	
1595			1600			1605			
Asn Val	Arg Thr	Asp Cys	Asn	His Ile	Phe Leu	Asn	Phe Val	Pro	
1610			1615			1620			
Thr Val	Ile Met	Asp Pro	Asn	Lys Ile	Glu Glu	Ser	Val Arg	Tyr	
1625			1630			1635			
Met Val	Met Arg	Tyr Gly	Ser	Arg Leu	Trp Lys	Leu	Arg Val	Leu	
1640			1645			1650			
Gln Ala	Glu Val	Lys Ile	Asn	Ile Arg	Gln Thr	Thr	Thr Gly	Ser	
1655			1660			1665			
Ala Val	Pro Ile	Arg Leu	Phe	Ile Thr	Asn Glu	Ser	Gly Tyr	Tyr	
1670			1675			1680			
Leu Asp	Ile Ser	Leu Tyr	Lys	Glu Val	Thr Asp	Ser	Arg Ser	Gly	
1685			1690			1695			
Asn Ile	Met Phe	His Ser	Phe	Gly Asn	Lys Gln	Gly	Pro Gln	His	
1700			1705			1710			
Gly Met	Leu Ile	Asn Thr	Pro	Tyr Val	Thr Lys	Asp	Leu Leu	Gln	
1715			1720			1725			
Ala Lys	Arg Phe	Gln Ala	Gln	Thr Leu	Gly Thr	Thr	Tyr Ile	Tyr	
1730			1735			1740			
Asp Phe	Pro Glu	Met Phe	Arg	Gln Ala	Leu Phe	Lys	Leu Trp	Gly	
1745			1750			1755			
Ser Pro	Asp Lys	Tyr Pro	Lys	Asp Ile	Leu Thr	Tyr	Thr Glu	Leu	
1760			1765			1770			
Val Leu	Asp Ser	Gln Gly	Gln	Leu Val	Glu Met	Asn	Arg Leu	Pro	
1775			1780			1785			
Gly Gly	Asn Glu	Val Gly	Met	Val Ala	Phe Lys	Met	Arg Phe	Lys	
1790			1795			1800			
Thr Gln	Glu Tyr	Pro Glu	Gly	Arg Asp	Val Ile	Val	Ile Gly	Asn	
1805			1810			1815			

Asp	Ile	Thr	Phe	Arg	Ile	Gly	Ser	Phe	Gly	Pro	Gly	Glu	Asp	Leu
1820						1825					1830			
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1835						1840					1845			
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Ser	Leu	Val	Thr	Cys	Arg	Ala	Ile	Gly	Ile	Gly	Ala	Tyr	Leu	Val
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2015						2020					2025			
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Phe Gln Pro His His His His His His Leu Ser Pro His Pro Pro
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Gly Thr Val Asp Lys Lys Met Val Glu Lys Cys Trp Lys Leu Met Asp
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Lys Val Val Arg Leu Cys Gln Asn Pro Lys Leu Ala Leu Lys Asn Ser
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Pro Pro Tyr Ile Leu Asp Leu Leu Pro Asp Thr Tyr Gln His Leu Arg
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Glu Tyr Phe Arg Val Phe Met Glu Asn Leu Met Lys Lys Thr Lys Gln
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Thr Ile Ser Leu Phe Lys Glu Gly Lys Glu Arg Met Tyr Glu Glu Asn
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Ser Gln Pro Arg Arg Asn Leu Thr Lys Leu Ser Leu Ile Phe Ser His
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Met Leu Ala Glu Leu Lys Gly Ile Phe Pro Ser Gly Leu Phe Gln Gly
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Asp Thr Phe Arg Ile Thr Lys Ala Asp Ala Ala Glu Phe Trp Arg Lys
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Lys Ser Thr Ile Asp Leu Thr Cys Asn Asp Tyr Ile Ser Val Phe Glu
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 Tyr Leu Phe Pro Asp Gly Arg Asn Gln Asn Pro Asp Leu Thr Gly Leu
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Gln Arg Arg Pro Leu Pro Cys Thr Pro Gly Asp Cys Pro Ser Arg Asp
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 Gly Asn Leu Ala Ala Ala His Ala Asn Thr Gly Pro Glu Glu Ser Glu
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 Asn Glu Asp Asp Gly Tyr Asp Val Pro Lys Pro Pro Val Pro Ala Val
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 Ser Gln Val Pro Glu Arg Pro Pro Lys Pro Phe Pro Arg Arg Ile Asn
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Ala	Glu	Asn	Asp	Lys	Asp	Val	Lys	Ile	Glu	Pro	Cys	Gly	His	Leu	Met	400
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Cys	Thr	Ser	Cys	Leu	Thr	Ser	Trp	Gln	Glu	Ser	Glu	Gly	Gln	Gly	Cys	415
cct	ttc	tgc	cga	tgt	gaa	att	aaa	ggt	act	gaa	ccc	atc	gtg	gta	gat	1296
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Pro	Phe	Asp	Pro	Arg	Gly	Ser	Gly	Ser	Leu	Leu	Arg	Gln	Gly	Ala	Glu	445
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Pro	Pro	Ser	Pro	Phe	Ser	Met	Ala	Pro	Gln	Ala	Ser	Leu	Pro	Pro	Val	495
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Gln	Arg	Arg	Pro	Leu	Pro	Cys	Thr	Pro	Gly	Asp	Cys	Pro	Ser	Arg	Asp	575
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Lys	Leu	Pro	Pro	Val	Pro	Ser	Ser	Arg	Leu	Gly	Asp	Ser	Trp	Leu	Pro	590
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Pro	Glu	Cys	Asp	His	Pro	Lys	Ile	Lys	Pro	Ser	Ser	Ser	Ala	Asn	Ala	
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Gly	Glu	Gln	Cys	Glu	Gly	Glu	Glu	Asp	Thr	Glu	Tyr	Met	Thr	Pro	Ser	
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Ser	Arg	Pro	Leu	Arg	Pro	Leu	Asp	Thr	Ser	Gln	Ser	Ser	Arg	Ala	Cys	
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Ile	Gln	Ser	Gln	Ala	Pro	Ser	Ile	Thr	Glu	Ser	Ser	Thr	Phe	Gly	Glu	
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Ser	Gln	Val	Pro	Glu	Arg	Pro	Pro	Lys	Pro	Phe	Pro	Arg	Arg	Ile	Asn	
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tct	gaa	cgg	aaa	gct	ggc	agc	tgt	cag	caa	ggg	agt	ggg	cct	gcc	gcc	2544
Ser	Glu	Arg	Lys	Ala	Gly	Ser	Cys	Gln	Gln	Gly	Ser	Gly	Pro	Ala	Ala	
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tct	gct	gcc	acc	gcc	tca	cct	cag	ctc	tcc	agt	gag	atc	gag	aac	ctc	2592
Ser	Ala	Ala	Thr	Ala	Ser	Pro	Gln	Leu	Ser	Ser	Glu	Ile	Glu	Asn	Leu	
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atg	agt	cag	ggg	tac	tcc	tac	cag	gac	atc	cag	aaa	gct	ttg	gtc	att	2640
Met	Ser	Gln	Gly	Tyr	Ser	Tyr	Gln	Asp	Ile	Gln	Lys	Ala	Leu	Val	Ile	
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gcc	cag	aac	aac	atc	gag	atg	gcc	aaa	aac	atc	ctc	cgg	gaa	ttt	gtt	2688
Ala	Gln	Asn	Asn	Ile	Glu	Met	Ala	Lys	Asn	Ile	Leu	Arg	Glu	Phe	Val	
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tcc	att	tct	tct	cct	gcc	cat	gta	gct	acc	tag						2721
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Gly Thr Val Asp Lys Lys Met Val Glu Lys Cys Trp Lys Leu Met Asp
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Lys Val Val Arg Leu Cys Gln Asn Pro Lys Leu Ala Leu Lys Asn Ser
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Pro Pro Tyr Ile Leu Asp Leu Leu Pro Asp Thr Tyr Gln His Leu Arg
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Thr Ile Leu Ser Arg Tyr Glu Gly Lys Met Glu Thr Leu Gly Glu Asn
 100 105 110

Glu Tyr Phe Arg Val Phe Met Glu Asn Leu Met Lys Lys Thr Lys Gln
 115 120 125

Thr Ile Ser Leu Phe Lys Glu Gly Lys Glu Arg Met Tyr Glu Glu Asn
 130 135 140

Ser Gln Pro Arg Arg Asn Leu Thr Lys Leu Ser Leu Ile Phe Ser His
 145 150 155 160

Met Leu Ala Glu Leu Lys Gly Ile Phe Pro Ser Gly Leu Phe Gln Gly
 165 170 175

Asp Thr Phe Arg Ile Thr Lys Ala Asp Ala Ala Glu Phe Trp Arg Lys
 180 185 190

Ala Phe Gly Glu Lys Thr Ile Val Pro Trp Lys Ser Phe Arg Gln Ala
 195 200 205

Leu His Glu Val His Pro Ile Ser Ser Gly Leu Glu Ala Met Ala Leu
 210 215 220

Lys Ser Thr Ile Asp Leu Thr Cys Asn Asp Tyr Ile Ser Val Phe Glu
225 230 235 240

Phe Asp Ile Phe Thr Arg Leu Phe Gln Pro Trp Ser Ser Leu Leu Arg
245 250 255

Asn Trp Asn Ser Leu Ala Val Thr His Pro Gly Tyr Met Ala Phe Leu
260 265 270

Thr Tyr Asp Glu Val Lys Ala Arg Leu Gln Lys Phe Ile His Lys Pro
275 280 285

Gly Ser Tyr Ile Phe Arg Leu Ser Cys Thr Arg Leu Gly Gln Trp Ala
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Ile Gly Tyr Val Thr Ala Asp Gly Asn Ile Leu Gln Thr Ile Pro His
305 310 315 320

Asn Lys Pro Leu Phe Gln Ala Leu Ile Asp Gly Phe Arg Glu Gly Phe
325 330 335

Tyr Leu Phe Pro Asp Gly Arg Asn Gln Asn Pro Asp Leu Thr Gly Leu
340 345 350

Cys Glu Pro Thr Pro Gln Asp His Ile Lys Val Thr Gln Glu Gln Tyr
355 360 365

Glu Leu Tyr Cys Glu Met Gly Ser Thr Phe Gln Leu Ala Lys Ile Cys
370 375 380

Ala Glu Asn Asp Lys Asp Val Lys Ile Glu Pro Cys Gly His Leu Met
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Cys Thr Ser Cys Leu Thr Ser Trp Gln Glu Ser Glu Gly Gln Gly Cys
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Pro Phe Cys Arg Cys Glu Ile Lys Gly Thr Glu Pro Ile Val Val Asp
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Pro Phe Asp Pro Arg Gly Ser Gly Ser Leu Leu Arg Gln Gly Ala Glu
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Asp Thr Leu Phe Met Met Lys Glu Leu Ala Gly Ala Lys Val Glu Arg
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Pro Pro Ser Pro Phe Ser Met Ala Pro Gln Ala Ser Leu Pro Pro Val
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Pro Pro Arg Leu Asp Leu Leu Pro Gln Arg Val Cys Val Pro Ser Ser
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Lys Asp Lys Pro Leu Pro Val Pro Pro Thr Leu Arg Asp Leu Pro Pro
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Pro Pro Pro Pro Asp Arg Pro Tyr Ser Val Gly Ala Glu Ser Arg Pro
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Gln Arg Arg Pro Leu Pro Cys Thr Pro Gly Asp Cys Pro Ser Arg Asp
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Lys Leu Pro Pro Val Pro Ser Ser Arg Leu Gly Asp Ser Trp Leu Pro
 580 585 590

Arg Pro Ile Pro Lys Val Pro Val Ser Ala Pro Ser Ser Ser Asp Pro
 595 600 605

Trp Thr Gly Arg Glu Leu Thr Asn Arg His Ser Leu Pro Phe Ser Leu
 610 615 620

Pro Ser Gln Met Glu Pro Arg Pro Asp Val Pro Arg Leu Gly Ser Thr
 625 630 635 640

Phe Ser Leu Asp Thr Ser Met Ser Met Asn Ser Ser Pro Leu Val Gly
 645 650 655

Pro Glu Cys Asp His Pro Lys Ile Lys Pro Ser Ser Ser Ala Asn Ala
 660 665 670

Ile Tyr Ser Leu Ala Ala Arg Pro Leu Pro Val Pro Lys Leu Pro Pro
 675 680 685

Gly Glu Gln Cys Glu Gly Glu Glu Asp Thr Glu Tyr Met Thr Pro Ser
 690 695 700

Ser Arg Pro Leu Arg Pro Leu Asp Thr Ser Gln Ser Ser Arg Ala Cys
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Asp Cys Asp Gln Gln Ile Asp Ser Cys Thr Tyr Glu Ala Met Tyr Asn
 725 730 735

Ile Gln Ser Gln Ala Pro Ser Ile Thr Glu Ser Ser Thr Phe Gly Glu
 740 745 750

Gly Asn Leu Ala Ala Ala His Ala Asn Thr Gly Pro Glu Glu Ser Glu
 755 760 765

Asn Glu Asp Asp Gly Tyr Asp Val Pro Lys Pro Pro Val Pro Ala Val
770 775 780

Leu Ala Arg Arg Thr Leu Ser Asp Ile Ser Asn Ala Ser Ser Ser Phe
785 790 795 800

Gly Trp Leu Ser Leu Asp Gly Asp Pro Thr Thr Asn Val Thr Glu Gly
805 810 815

Ser Gln Val Pro Glu Arg Pro Pro Lys Pro Phe Pro Arg Arg Ile Asn
820 825 830

Ser Glu Arg Lys Ala Gly Ser Cys Gln Gln Gly Ser Gly Pro Ala Ala
835 840 845

Ser Ala Ala Thr Ala Ser Pro Gln Leu Ser Ser Glu Ile Glu Asn Leu
850 855 860

Met Ser Gln Gly Tyr Ser Tyr Gln Asp Ile Gln Lys Ala Leu Val Ile
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Phe Gln Pro His His His His His His His Leu Ser Pro His Pro Pro
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acc ata agc ctc ttc aag gag gga aaa gaa aga atg tat gag gag aat Thr Ile Ser Leu Phe Lys Glu Gly Lys Glu Arg Met Tyr Glu Glu Asn 130 135 140	432
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Ser Gly Gly Ser Gly Ser Gly Gly Leu Ile Gly Leu Met Lys Asp Ala
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Phe Gln Pro His His His His His His Leu Ser Pro His Pro Pro
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Gly Thr Val Asp Lys Lys Met Val Glu Lys Cys Trp Lys Leu Met Asp
 50 55 60

Lys Val Val Arg Leu Cys Gln Asn Pro Lys Leu Ala Leu Lys Asn Ser
 65 70 75 80

Pro Pro Tyr Ile Leu Asp Leu Leu Pro Asp Thr Tyr Gln His Leu Arg
 85 90 95

Thr Ile Leu Ser Arg Tyr Glu Gly Lys Met Glu Thr Leu Gly Glu Asn
 100 105 110

Glu Tyr Phe Arg Val Phe Met Glu Asn Leu Met Lys Lys Thr Lys Gln
 115 120 125

Thr Ile Ser Leu Phe Lys Glu Gly Lys Glu Arg Met Tyr Glu Glu Asn
 130 135 140

Ser Gln Pro Arg Arg Asn Leu Thr Lys Leu Ser Leu Ile Phe Ser His
 145 150 155 160

Met Leu Ala Glu Leu Lys Gly Ile Phe Pro Ser Gly Leu Phe Gln Gly

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180	185	190
Ala Phe Gly Glu Lys Thr Ile Val Pro Trp Lys Ser Phe Arg Gln Ala		
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Leu His Glu Val His Pro Ile Ser Ser Gly Leu Glu Ala Met Ala Leu		
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Lys Ser Thr Ile Asp Leu Thr Cys Asn Asp Tyr Ile Ser Val Phe Glu		
225	230	235
Phe Asp Ile Phe Thr Arg Leu Phe Gln Pro Trp Ser Ser Leu Leu Arg		
245	250	255
Asn Trp Asn Ser Leu Ala Val Thr His Pro Gly Tyr Met Ala Phe Leu		
260	265	270
Thr Tyr Asp Glu Val Lys Ala Arg Leu Gln Lys Phe Ile His Lys Pro		
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Gly Ser Tyr Ile Phe Arg Leu Ser Cys Thr Arg Leu Gly Gln Trp Ala		
290	295	300
Ile Gly Tyr Val Thr Ala Asp Gly Asn Ile Leu Gln Thr Ile Pro His		
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Asn Lys Pro Leu Phe Gln Ala Leu Ile Asp Gly Phe Arg Glu Gly Phe		
325	330	335
Tyr Leu Phe Pro Asp Gly Arg Asn Gln Asn Pro Asp Leu Thr Gly Leu		
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Cys Glu Pro Thr Pro Gln Asp His Ile Lys Val Thr Gln Glu Gln Tyr		
355	360	365
Glu Leu Tyr Cys Glu Met Gly Ser Thr Phe Gln Leu Cys Lys Ile Cys		
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Cys Thr Ser Cys Leu Thr Ser Trp Gln Glu Ser Glu Gly Gln Gly Cys		
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Pro Phe Cys Arg Cys Glu Ile Lys Gly Thr Glu Pro Ile Val Val Asp		
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Pro Phe Asp Pro Arg Gly Ser Gly Ser Leu Leu Arg Gln Gly Ala Glu		

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Lys Asp Lys Pro Leu Pro Val Pro Pro Thr Leu Arg Asp Leu Pro Pro 530 535 540		
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Gln Arg Arg Pro Leu Pro Cys Thr Pro Gly Asp Cys Pro Ser Arg Asp 565 570 575		
Lys Leu Pro Pro Val Pro Ser Ser Arg Leu Gly Asp Ser Trp Leu Pro 580 585 590		
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Pro Ser Gln Met Glu Pro Arg Pro Asp Val Pro Arg Leu Gly Ser Thr 625 630 635 640		
Phe Ser Leu Asp Thr Ser Met Ser Met Asn Ser Ser Pro Leu Val Gly 645 650 655		
Pro Glu Cys Asp His Pro Lys Ile Lys Pro Ser Ser Ser Ala Asn Ala 660 665 670		
Ile Tyr Ser Leu Ala Ala Arg Pro Leu Pro Val Pro Lys Leu Pro Pro 675 680 685		
Gly Glu Gln Cys Glu Gly Glu Glu Asp Thr Glu Phe Met Thr Pro Ser 690 695 700		

Ser Arg Pro Leu Arg Pro Leu Asp Thr Ser Gln Ser Ser Arg Ala Cys
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Asp Cys Asp Gln Gln Ile Asp Ser Cys Thr Tyr Glu Ala Met Tyr Asn
725 730 735

Ile Gln Ser Gln Ala Pro Ser Ile Thr Glu Ser Ser Thr Phe Gly Glu
740 745 750

Gly Asn Leu Ala Ala Ala His Ala Asn Thr Gly Pro Glu Glu Ser Glu
755 760 765

Asn Glu Asp Asp Gly Tyr Asp Val Pro Lys Pro Pro Val Pro Ala Val
770 775 780

Leu Ala Arg Arg Thr Leu Ser Asp Ile Ser Asn Ala Ser Ser Ser Phe
785 790 795 800

Gly Trp Leu Ser Leu Asp Gly Asp Pro Thr Thr Asn Val Thr Glu Gly
805 810 815

Ser Gln Val Pro Glu Arg Pro Pro Lys Pro Phe Pro Arg Arg Ile Asn
820 825 830

Ser Glu Arg Lys Ala Gly Ser Cys Gln Gln Gly Ser Gly Pro Ala Ala
835 840 845

Ser Ala Ala Thr Ala Ser Pro Gln Leu Ser Ser Glu Ile Glu Asn Leu
850 855 860

Met Ser Gln Gly Tyr Ser Tyr Gln Asp Ile Gln Lys Ala Leu Val Ile
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Ser Gly Gly Ser Gly Ser Gly Gly Leu Ile Gly Leu Met Lys Asp Ala	
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ttc cag ccg cac cac cac cac cac ctc agc ccc cac ccg ccg	144
Phe Gln Pro His His His His His Leu Ser Pro His Pro Pro	
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Gly Thr Val Asp Lys Lys Met Val Glu Lys Cys Trp Lys Leu Met Asp	
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Lys Val Val Arg Leu Cys Gln Asn Pro Lys Leu Ala Leu Lys Asn Ser	
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Pro Pro Tyr Ile Leu Asp Leu Leu Pro Asp Thr Tyr Gln His Leu Arg	
85 90 95	
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Thr Ile Leu Ser Arg Tyr Glu Gly Lys Met Glu Thr Leu Gly Glu Asn	
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gag tat ttt agg gtg ttt atg gag aat ttg atg aag aaa act aag caa	384
Glu Tyr Phe Arg Val Phe Met Glu Asn Leu Met Lys Lys Thr Lys Gln	
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acc ata agc ctc ttc aag gag gga aaa gaa aga atg tat gag gag aat	432
Thr Ile Ser Leu Phe Lys Glu Gly Lys Glu Arg Met Tyr Glu Glu Asn	
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Ser Gln Pro Arg Arg Asn Leu Thr Lys Leu Ser Leu Ile Phe Ser His	
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Met Leu Ala Glu Leu Lys Gly Ile Phe Pro Ser Gly Leu Phe Gln Gly	
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Leu His Glu Val His Pro Ile Ser Ser Gly Leu Glu Ala Met Ala Leu	
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 Ser Ala Ala Thr Ala Ser Pro Gln Leu Ser Ser Glu Ile Glu Asn Leu
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Gly Thr Val Asp Lys Lys Met Val Glu Lys Cys Trp Lys Leu Met Asp
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Lys Val Val Arg Leu Cys Gln Asn Pro Lys Leu Ala Leu Lys Asn Ser
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Pro Pro Tyr Ile Leu Asp Leu Leu Pro Asp Thr Tyr Gln His Leu Arg
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Thr Ile Leu Ser Arg Tyr Glu Gly Lys Met Glu Thr Leu Gly Glu Asn
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Glu Tyr Phe Arg Val Phe Met Glu Asn Leu Met Lys Lys Thr Lys Gln
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Thr Ile Ser Leu Phe Lys Glu Gly Lys Glu Arg Met Tyr Glu Glu Asn
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Ser Gln Pro Arg Arg Asn Leu Thr Lys Leu Ser Leu Ile Phe Ser His
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Met Leu Ala Glu Leu Lys Gly Ile Phe Pro Ser Gly Leu Phe Gln Gly
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Asp Thr Phe Arg Ile Thr Lys Ala Asp Ala Ala Glu Phe Trp Arg Lys
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Ile Gly Tyr Val Thr Ala Asp Gly Asn Ile Leu Gln Thr Ile Pro His
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Tyr Leu Phe Pro Asp Gly Arg Asn Gln Asn Pro Asp Leu Thr Gly Leu
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Cys Glu Pro Thr Pro Gln Asp His Ile Lys Val Thr Gln Glu Gln Tyr
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Gly Asn Leu Ala Ala Ala His Ala Asn Thr Gly Pro Glu Glu Ser Glu
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Asn Glu Asp Asp Gly Tyr Asp Val Pro Lys Pro Pro Val Pro Ala Val
770 775 780

Leu Ala Arg Arg Thr Leu Ser Asp Ile Ser Asn Ala Ser Ser Ser Phe
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Ser Glu Arg Lys Ala Gly Ser Cys Gln Gln Gly Ser Gly Pro Ala Ala
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Met Ser Gln Gly Tyr Ser Tyr Gln Asp Ile Gln Lys Ala Leu Val Ile
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Phe Gln Pro His His His His His His Leu Ser Pro His Pro Pro	
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Gly Thr Val Asp Lys Lys Met Val Glu Lys Cys Trp Lys Leu Met Asp	
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Lys Val Val Arg Leu Cys Gln Asn Pro Lys Leu Ala Leu Lys Asn Ser	
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Pro Pro Tyr Ile Leu Asp Leu Leu Pro Asp Thr Tyr Gln His Leu Arg	
85 90 95	

act atc ttg tca aga tat gag ggg aag atg gag aca ctt gga gaa aat	336
Thr Ile Leu Ser Arg Tyr Glu Gly Lys Met Glu Thr Leu Gly Glu Asn	
100 105 110	

gag tat ttt agg gtg ttt atg gag aat ttg atg aag aaa act aag caa	384
Glu Tyr Phe Arg Val Phe Met Glu Asn Leu Met Lys Lys Thr Lys Gln	
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acc ata agc ctc ttc aag gag gga aaa gaa aga atg tat gag gag aat	432
Thr Ile Ser Leu Phe Lys Glu Gly Lys Glu Arg Met Tyr Glu Glu Asn	
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Met Leu Ala Glu Leu Lys Gly Ile Phe Pro Ser Gly Leu Phe Gln Gly	
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Phe	Gln	Pro	His	His	His	His	His	His	His	Leu	Ser	Pro	His	Pro	Pro		
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Glu Tyr Phe Arg Val Phe Met Glu Asn Leu Met Lys Lys Thr Lys Gln
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Thr Ile Ser Leu Phe Lys Glu Gly Lys Glu Arg Met Tyr Glu Glu Asn
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Ser Gln Pro Arg Arg Asn Leu Thr Lys Leu Ser Leu Ile Phe Ser His
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Met Leu Ala Glu Leu Lys Gly Ile Phe Pro Ser Gly Leu Phe Gln Gly
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Asp Thr Phe Arg Ile Thr Lys Ala Asp Ala Ala Glu Phe Trp Arg Lys
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Ala Phe Gly Glu Lys Thr Ile Val Pro Trp Lys Ser Phe Arg Gln Ala
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Leu His Glu Val His Pro Ile Ser Ser Gly Leu Glu Ala Met Ala Leu
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Lys Ser Thr Ile Asp Leu Thr Cys Asn Asp Tyr Ile Ser Val Phe Glu
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Phe Asp Ile Phe Thr Arg Leu Phe Gln Pro Trp Ser Ser Leu Leu Arg
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Ile Gly Tyr Val Thr Ala Asp Gly Asn Ile Leu Gln Thr Ile Pro His
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Asn Lys Pro Leu Phe Gln Ala Leu Ile Asp Gly Phe Arg Glu Gly Phe
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 Tyr Leu Phe Pro Asp Gly Arg Asn Gln Asn Pro Asp Leu Thr Gly Leu
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 Cys Glu Pro Thr Pro Gln Asp His Ile Lys Val Thr Gln Glu Gln Tyr
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 Lys Asp Lys Pro Leu Pro Val Pro Pro Thr Leu Arg Asp Leu Pro Pro
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 Gln Arg Arg Pro Leu Pro Cys Thr Pro Gly Asp Cys Pro Ser Arg Asp
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 Lys Leu Pro Pro Val Pro Ser Ser Arg Leu Gly Asp Ser Trp Leu Pro
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Arg Pro Ile Pro Lys Val Pro Val Ser Ala Pro Ser Ser Ser Asp Pro
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Trp Thr Gly Arg Glu Leu Thr Asn Arg His Ser Leu Pro Phe Ser Leu
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Pro Ser Gln Met Glu Pro Arg Pro Asp Val Pro Arg Leu Gly Ser Thr
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 645 650 655

Pro Glu Cys Asp His Pro Lys Ile Lys Pro Ser Ser Ser Ala Asn Ala
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Gly Glu Gln Cys Glu Gly Glu Glu Asp Thr Glu Tyr Met Thr Pro Ser
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Ser Arg Pro Leu Arg Pro Leu Asp Thr Ser Gln Ser Ser Arg Ala Cys
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Asp Cys Asp Gln Gln Ile Asp Ser Cys Thr Tyr Glu Ala Met Tyr Asn
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Ile Gln Ser Gln Ala Pro Ser Ile Thr Glu Ser Ser Thr Phe Gly Glu
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Gly Asn Leu Ala Ala Ala His Ala Asn Thr Gly Pro Glu Glu Ser Glu
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Asn Glu Asp Asp Gly Phe Asp Val Pro Lys Pro Pro Val Pro Ala Val
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Leu Ala Arg Arg Thr Leu Ser Asp Ile Ser Asn Ala Ser Ser Ser Phe
 785 790 795 800

Gly Trp Leu Ser Leu Asp Gly Asp Pro Thr Thr Asn Val Thr Glu Gly
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Ser Gln Val Pro Glu Arg Pro Pro Lys Pro Phe Pro Arg Arg Ile Asn
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Ser Glu Arg Lys Ala Gly Ser Cys Gln Gln Gly Ser Gly Pro Ala Ala
 835 840 845

Ser Ala Ala Thr Ala Ser Pro Gln Leu Ser Ser Glu Ile Glu Asn Leu
 850 855 860

Met Ser Gln Gly Tyr Ser Tyr Gln Asp Ile Gln Lys Ala Leu Val Ile
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Phe Gln Pro His His His His His His His Leu Ser Pro His Pro Pro	
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Gly Thr Val Asp Lys Lys Met Val Glu Lys Cys Trp Lys Leu Met Asp	
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Lys Val Val Arg Leu Cys Gln Asn Pro Lys Leu Ala Leu Lys Asn Ser	
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Glu Tyr Phe Arg Val Phe Met Glu Asn Leu Met Lys Lys Thr Lys Gln	
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	450					455					460					
gat	act	ctc	ttc	atg	atg	aag	gaa	ttg	gct	ggc	gcc	aag	gtg	gaa	cgg	1440
Asp	Thr	Leu	Phe	Met	Met	Lys	Glu	Leu	Ala	Gly	Ala	Lys	Val	Glu	Arg	
	465				470					475					480	
ccg	cct	tct	cca	ttc	tcc	atg	gcc	cca	caa	gct	tcc	ctt	ccc	ccg	gtg	1488
Pro	Pro	Ser	Pro	Phe	Ser	Met	Ala	Pro	Gln	Ala	Ser	Leu	Pro	Pro	Val	
				485					490					495		
cca	cca	cga	ctt	gac	ctt	ctg	ccg	cag	cga	gta	tgt	gtt	ccc	tca	agt	1536
Pro	Pro	Arg	Leu	Asp	Leu	Leu	Pro	Gln	Arg	Val	Cys	Val	Pro	Ser	Ser	
			500					505					510			
gct	tct	gct	ctt	gga	act	gct	tct	aag	gct	gct	tct	ggc	tcc	ctt	cat	1584
Ala	Ser	Ala	Leu	Gly	Thr	Ala	Ser	Lys	Ala	Ala	Ser	Gly	Ser	Leu	His	
		515					520					525				
aaa	gac	aaa	cca	ttg	cca	gta	cct	ccc	aca	ctt	cga	gat	ctt	cca	cca	1632
Lys	Asp	Lys	Pro	Leu	Pro	Val	Pro	Pro	Thr	Leu	Arg	Asp	Leu	Pro	Pro	
	530					535					540					
cca	ccg	cct	cca	gac	cgg	cca	tat	tct	gtt	gga	gca	gaa	tcc	cga	cct	1680
Pro	Pro	Pro	Pro	Asp	Arg	Pro	Tyr	Ser	Val	Gly	Ala	Glu	Ser	Arg	Pro	
	545				550					555					560	
caa	aga	cgc	ccc	ttg	cct	tgt	aca	cca	ggc	gac	tgt	ccc	tcc	aga	gac	1728
Gln	Arg	Arg	Pro	Leu	Pro	Cys	Thr	Pro	Gly	Asp	Cys	Pro	Ser	Arg	Asp	
				565					570					575		
aaa	ctg	ccc	cct	gtc	ccc	tct	agc	cgc	ctt	gga	gac	tca	tgg	ctg	ccc	1776
Lys	Leu	Pro	Pro	Val	Pro	Ser	Ser	Arg	Leu	Gly	Asp	Ser	Trp	Leu	Pro	
			580					585					590			
cgg	cca	atc	ccc	aaa	gta	cca	gta	tct	gcc	cca	agt	tcc	agt	gat	ccc	1824
Arg	Pro	Ile	Pro	Lys	Val	Pro	Val	Ser	Ala	Pro	Ser	Ser	Ser	Asp	Pro	
		595					600					605				
tgg	aca	gga	aga	gaa	tta	acc	aac	cgg	cac	tca	ctt	cca	ttt	tca	ttg	1872
Trp	Thr	Gly	Arg	Glu	Leu	Thr	Asn	Arg	His	Ser	Leu	Pro	Phe	Ser	Leu	
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ccc	tca	caa	atg	gag	ccc	aga	cca	gat	gtg	cct	agg	ctc	gga	agc	acg	1920
Pro	Ser	Gln	Met	Glu	Pro	Arg	Pro	Asp	Val	Pro	Arg	Leu	Gly	Ser	Thr	
	625				630				635						640	
ttc	agt	ctg	gat	acc	tcc	atg	agt	atg	aat	agc	agc	cca	tta	gta	ggc	1968
Phe	Ser	Leu	Asp	Thr	Ser	Met	Ser	Met	Asn	Ser	Ser	Pro	Leu	Val	Gly	
				645					650					655		
cca	gag	tgt	gac	cac	ccc	aaa	atc	aaa	cct	tcc	tca	tct	gcc	aat	gcc	2016
Pro	Glu	Cys	Asp	His	Pro	Lys	Ile	Lys	Pro	Ser	Ser	Ser	Ala	Asn	Ala	
			660					665					670			
att	tat	tct	ctg	gct	gcc	aga	cct	ctt	cct	gtg	cca	aaa	ctg	cca	cct	2064

Ile	Tyr	Ser	Leu	Ala	Ala	Arg	Pro	Leu	Pro	Val	Pro	Lys	Leu	Pro	Pro		
		675					680					685					
ggg	gag	caa	tgt	gag	ggt	gaa	gag	gac	aca	gag	ttc	atg	act	ccc	tct	2112	
Gly	Glu	Gln	Cys	Glu	Gly	Glu	Glu	Asp	Thr	Glu	Phe	Met	Thr	Pro	Ser		
	690					695					700						
tcc	agg	cct	cta	cgg	cct	ttg	gat	aca	tcc	cag	agt	tca	cga	gca	tgt	2160	
Ser	Arg	Pro	Leu	Arg	Pro	Leu	Asp	Thr	Ser	Gln	Ser	Ser	Arg	Ala	Cys		
705					710					715					720		
gat	tgc	gac	cag	cag	att	gat	agc	tgt	acg	ttt	gaa	gca	atg	tat	aat	2208	
Asp	Cys	Asp	Gln	Gln	Ile	Asp	Ser	Cys	Thr	Phe	Glu	Ala	Met	Tyr	Asn		
				725					730					735			
att	cag	tcc	cag	gcg	cca	tct	atc	acc	gag	agc	agc	acc	ttt	ggg	gaa	2256	
Ile	Gln	Ser	Gln	Ala	Pro	Ser	Ile	Thr	Glu	Ser	Ser	Thr	Phe	Gly	Glu		
			740					745					750				
ggg	aat	ttg	gcc	gca	gcc	cat	gcc	aac	act	ggg	ccc	gag	gag	tca	gaa	2304	
Gly	Asn	Leu	Ala	Ala	Ala	His	Ala	Asn	Thr	Gly	Pro	Glu	Glu	Ser	Glu		
		755					760					765					
aat	gag	gat	gat	ggg	ttt	gat	gtc	cca	aag	cca	cct	gtg	ccg	gcc	gtg	2352	
Asn	Glu	Asp	Asp	Gly	Phe	Asp	Val	Pro	Lys	Pro	Pro	Val	Pro	Ala	Val		
	770					775					780						
ctg	gcc	cgc	cga	act	ctc	tca	gat	atc	tct	aat	gcc	agc	tcc	tcc	ttt	2400	
Leu	Ala	Arg	Arg	Thr	Leu	Ser	Asp	Ile	Ser	Asn	Ala	Ser	Ser	Ser	Phe		
785					790					795					800		
ggc	tgg	ttg	tct	ctg	gat	ggt	gat	cct	aca	aca	aat	gtc	act	gaa	ggg	2448	
Gly	Trp	Leu	Ser	Leu	Asp	Gly	Asp	Pro	Thr	Thr	Asn	Val	Thr	Glu	Gly		
				805					810					815			
tcc	caa	gtt	ccc	gag	agg	cct	cca	aaa	cca	ttc	ccg	cgg	aga	atc	aac	2496	
Ser	Gln	Val	Pro	Glu	Arg	Pro	Pro	Lys	Pro	Phe	Pro	Arg	Arg	Ile	Asn		
			820					825					830				
tct	gaa	cgg	aaa	gct	ggc	agc	tgt	cag	caa	ggg	agt	ggg	cct	gcc	gcc	2544	
Ser	Glu	Arg	Lys	Ala	Gly	Ser	Cys	Gln	Gln	Gly	Ser	Gly	Pro	Ala	Ala		
		835					840					845					
tct	gct	gcc	acc	gcc	tca	cct	cag	ctc	tcc	agt	gag	atc	gag	aac	ctc	2592	
Ser	Ala	Ala	Thr	Ala	Ser	Pro	Gln	Leu	Ser	Ser	Glu	Ile	Glu	Asn	Leu		
	850					855					860						
atg	agt	cag	ggg	tac	tcc	tac	cag	gac	atc	cag	aaa	gct	ttg	gtc	att	2640	
Met	Ser	Gln	Gly	Tyr	Ser	Tyr	Gln	Asp	Ile	Gln	Lys	Ala	Leu	Val	Ile		
	865				870					875					880		
gcc	cag	aac	aac	atc	gag	atg	gcc	aaa	aac	atc	ctc	cgg	gaa	ttt	gtt	2688	
Ala	Gln	Asn	Asn	Ile	Glu	Met	Ala	Lys	Asn	Ile	Leu	Arg	Glu	Phe	Val		
				885				890						895			
tcc	att	tct	tct	cct	gcc	cat	gta	gct	aat	tag						2721	
Ser	Ile	Ser	Ser	Pro	Ala	His	Val	Ala	Thr								
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<212> PRT

<213> c-Cbl Y700F/Y731F/Y774F

<400> 260

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Ser Gly Gly Ser Gly Ser Gly Gly Leu Ile Gly Leu Met Lys Asp Ala
20 25 30

Phe Gln Pro His His His His His His Leu Ser Pro His Pro Pro
35 40 45

Gly Thr Val Asp Lys Lys Met Val Glu Lys Cys Trp Lys Leu Met Asp
50 55 60

Lys Val Val Arg Leu Cys Gln Asn Pro Lys Leu Ala Leu Lys Asn Ser
65 70 75 80

Pro Pro Tyr Ile Leu Asp Leu Leu Pro Asp Thr Tyr Gln His Leu Arg
85 90 95

Thr Ile Leu Ser Arg Tyr Glu Gly Lys Met Glu Thr Leu Gly Glu Asn
100 105 110

Glu Tyr Phe Arg Val Phe Met Glu Asn Leu Met Lys Lys Thr Lys Gln
115 120 125

Thr Ile Ser Leu Phe Lys Glu Gly Lys Glu Arg Met Tyr Glu Glu Asn
130 135 140

Ser Gln Pro Arg Arg Asn Leu Thr Lys Leu Ser Leu Ile Phe Ser His
145 150 155 160

Met Leu Ala Glu Leu Lys Gly Ile Phe Pro Ser Gly Leu Phe Gln Gly
165 170 175

Asp Thr Phe Arg Ile Thr Lys Ala Asp Ala Ala Glu Phe Trp Arg Lys
180 185 190

Ala Phe Gly Glu Lys Thr Ile Val Pro Trp Lys Ser Phe Arg Gln Ala
195 200 205

Leu His Glu Val His Pro Ile Ser Ser Gly Leu Glu Ala Met Ala Leu
210 215 220

Lys Ser Thr Ile Asp Leu Thr Cys Asn Asp Tyr Ile Ser Val Phe Glu
225 230 235 240

Phe Asp Ile Phe Thr Arg Leu Phe Gln Pro Trp Ser Ser Leu Leu Arg
245 250 255

Asn Trp Asn Ser Leu Ala Val Thr His Pro Gly Tyr Met Ala Phe Leu
260 265 270

Thr Tyr Asp Glu Val Lys Ala Arg Leu Gln Lys Phe Ile His Lys Pro
275 280 285

Gly Ser Tyr Ile Phe Arg Leu Ser Cys Thr Arg Leu Gly Gln Trp Ala
290 295 300

Ile Gly Tyr Val Thr Ala Asp Gly Asn Ile Leu Gln Thr Ile Pro His
305 310 315 320

Asn Lys Pro Leu Phe Gln Ala Leu Ile Asp Gly Phe Arg Glu Gly Phe
325 330 335

Tyr Leu Phe Pro Asp Gly Arg Asn Gln Asn Pro Asp Leu Thr Gly Leu
340 345 350

Cys Glu Pro Thr Pro Gln Asp His Ile Lys Val Thr Gln Glu Gln Tyr
355 360 365

Glu Leu Tyr Cys Glu Met Gly Ser Thr Phe Gln Leu Cys Lys Ile Cys
370 375 380

Ala Glu Asn Asp Lys Asp Val Lys Ile Glu Pro Cys Gly His Leu Met
385 390 395 400

Cys Thr Ser Cys Leu Thr Ser Trp Gln Glu Ser Glu Gly Gln Gly Cys
405 410 415

Pro Phe Cys Arg Cys Glu Ile Lys Gly Thr Glu Pro Ile Val Val Asp
420 425 430

Pro Phe Asp Pro Arg Gly Ser Gly Ser Leu Leu Arg Gln Gly Ala Glu
435 440 445

Gly Ala Pro Ser Pro Asn Tyr Asp Asp Asp Asp Glu Arg Ala Asp
450 455 460

Asp Thr Leu Phe Met Met Lys Glu Leu Ala Gly Ala Lys Val Glu Arg
465 470 475 480

Pro Pro Ser Pro Phe Ser Met Ala Pro Gln Ala Ser Leu Pro Pro Val
485 490 495

Pro Pro Arg Leu Asp Leu Leu Pro Gln Arg Val Cys Val Pro Ser Ser
500 505 510

Ala Ser Ala Leu Gly Thr Ala Ser Lys Ala Ala Ser Gly Ser Leu His
515 520 525

Lys Asp Lys Pro Leu Pro Val Pro Pro Thr Leu Arg Asp Leu Pro Pro
 530 535 540

Pro Pro Pro Pro Asp Arg Pro Tyr Ser Val Gly Ala Glu Ser Arg Pro
 545 550 555 560

Gln Arg Arg Pro Leu Pro Cys Thr Pro Gly Asp Cys Pro Ser Arg Asp
 565 570 575

Lys Leu Pro Pro Val Pro Ser Ser Arg Leu Gly Asp Ser Trp Leu Pro
 580 585 590

Arg Pro Ile Pro Lys Val Pro Val Ser Ala Pro Ser Ser Ser Asp Pro
 595 600 605

Trp Thr Gly Arg Glu Leu Thr Asn Arg His Ser Leu Pro Phe Ser Leu
 610 615 620

Pro Ser Gln Met Glu Pro Arg Pro Asp Val Pro Arg Leu Gly Ser Thr
 625 630 635 640

Phe Ser Leu Asp Thr Ser Met Ser Met Asn Ser Ser Pro Leu Val Gly
 645 650 655

Pro Glu Cys Asp His Pro Lys Ile Lys Pro Ser Ser Ser Ala Asn Ala
 660 665 670

Ile Tyr Ser Leu Ala Ala Arg Pro Leu Pro Val Pro Lys Leu Pro Pro
 675 680 685

Gly Glu Gln Cys Glu Gly Glu Glu Asp Thr Glu Phe Met Thr Pro Ser
 690 695 700

Ser Arg Pro Leu Arg Pro Leu Asp Thr Ser Gln Ser Ser Arg Ala Cys
 705 710 715 720

Asp Cys Asp Gln Gln Ile Asp Ser Cys Thr Phe Glu Ala Met Tyr Asn
 725 730 735

Ile Gln Ser Gln Ala Pro Ser Ile Thr Glu Ser Ser Thr Phe Gly Glu
 740 745 750

Gly Asn Leu Ala Ala Ala His Ala Asn Thr Gly Pro Glu Glu Ser Glu
 755 760 765

Asn Glu Asp Asp Gly Phe Asp Val Pro Lys Pro Pro Val Pro Ala Val
 770 775 780

Leu Ala Arg Arg Thr Leu Ser Asp Ile Ser Asn Ala Ser Ser Ser Phe
 785 790 795 800

Gly Trp Leu Ser Leu Asp Gly Asp Pro Thr Thr Asn Val Thr Glu Gly
805 810 815

Ser Gln Val Pro Glu Arg Pro Pro Lys Pro Phe Pro Arg Arg Ile Asn
820 825 830

Ser Glu Arg Lys Ala Gly Ser Cys Gln Gln Gly Ser Gly Pro Ala Ala
835 840 845

Ser Ala Ala Thr Ala Ser Pro Gln Leu Ser Ser Glu Ile Glu Asn Leu
850 855 860

Met Ser Gln Gly Tyr Ser Tyr Gln Asp Ile Gln Lys Ala Leu Val Ile
865 870 875 880

Ala Gln Asn Asn Ile Glu Met Ala Lys Asn Ile Leu Arg Glu Phe Val
885 890 895

Ser Ile Ser Ser Pro Ala His Val Ala Thr
900 905

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<400> 261

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tcc ggg ggc tcg ggt tcg ggt ggc ctg att ggg ctc atg aag gac gcc	96
Ser Gly Gly Ser Gly Ser Gly Gly Leu Ile Gly Leu Met Lys Asp Ala	
20 25 30	
ttc cag ccg cac cac cac cac cac cac ctc agc ccc cac ccg ccg	144
Phe Gln Pro His His His His His His His Leu Ser Pro His Pro Pro	
35 40 45	
ggg acg gtg gac aag aag atg gtg gag aag tgc tgg aag ctc atg gac	192
Gly Thr Val Asp Lys Lys Met Val Glu Lys Cys Trp Lys Leu Met Asp	
50 55 60	
aag gtg gtg cgg ttg tgt cag aac cca aag ctg gcg cta aag aat agc	240
Lys Val Val Arg Leu Cys Gln Asn Pro Lys Leu Ala Leu Lys Asn Ser	
65 70 75 80	

cca cct tat atc tta gac ctg cta cca gat acc tac cag cat ctc cgt Pro Pro Tyr Ile Leu Asp Leu Leu Pro Asp Thr Tyr Gln His Leu Arg 85 90 95	288
act atc ttg tca aga tat gag ggg aag atg gag aca ctt gga gaa aat Thr Ile Leu Ser Arg Tyr Glu Gly Lys Met Glu Thr Leu Gly Glu Asn 100 105 110	336
gag tat ttt agg gtg ttt atg gag aat ttg atg aag aaa act aag caa Glu Tyr Phe Arg Val Phe Met Glu Asn Leu Met Lys Lys Thr Lys Gln 115 120 125	384
acc ata agc ctc ttc aag gag gga aaa gaa aga atg tat gag gag aat Thr Ile Ser Leu Phe Lys Glu Gly Lys Glu Arg Met Tyr Glu Glu Asn 130 135 140	432
tct cag cct agg cga aac cta acc aaa ctg tcc ctc atc ttc agc cac Ser Gln Pro Arg Arg Asn Leu Thr Lys Leu Ser Leu Ile Phe Ser His 145 150 155 160	480
atg ctg gca gaa cta aaa gga atc ttt cca agt gga ctc ttt cag gga Met Leu Ala Glu Leu Lys Gly Ile Phe Pro Ser Gly Leu Phe Gln Gly 165 170 175	528
gac aca ttt cgg att act aaa gca gat gct gcg gaa ttt tgg aga aaa Asp Thr Phe Arg Ile Thr Lys Ala Asp Ala Ala Glu Phe Trp Arg Lys 180 185 190	576
gct ttt ggg gaa aag aca ata gtc cct tgg aag agc ttt cga cag gct Ala Phe Gly Glu Lys Thr Ile Val Pro Trp Lys Ser Phe Arg Gln Ala 195 200 205	624
cta cat gaa gtg cat ccc atc agt tct ggg ctg gag gcc atg gct ctg Leu His Glu Val His Pro Ile Ser Ser Gly Leu Glu Ala Met Ala Leu 210 215 220	672
aaa tcc act att gat ctg acc tgc aat gat tat att tcg gtt ttt gaa Lys Ser Thr Ile Asp Leu Thr Cys Asn Asp Tyr Ile Ser Val Phe Glu 225 230 235 240	720
ttt gac atc ttt acc cga ctc ttt cag ccc tgg tcc tct ttg ctc agg Phe Asp Ile Phe Thr Arg Leu Phe Gln Pro Trp Ser Ser Leu Leu Arg 245 250 255	768
aat tgg aac agc ctt gct gta act cat cct ggc tac atg gct ttt ttg Asn Trp Asn Ser Leu Ala Val Thr His Pro Gly Tyr Met Ala Phe Leu 260 265 270	816
acg tat gac gaa gtg aaa gct cgg ctc cag aaa ttc att cac aaa cct Thr Tyr Asp Glu Val Lys Ala Arg Leu Gln Lys Phe Ile His Lys Pro 275 280 285	864
ggc agt tat atc ttc cgg ctg agc tgt act cgt ctg ggt cag tgg gct Gly Ser Tyr Ile Phe Arg Leu Ser Cys Thr Arg Leu Gly Gln Trp Ala 290 295 300	912
att ggg tat gtt act gct gat ggg aac att ctc cag aca atc cct cac Ile Gly Tyr Val Thr Ala Asp Gly Asn Ile Leu Gln Thr Ile Pro His 305 310 315 320	960
aat aaa cct ctc ttc caa gca ctg att gat ggc ttc agg gaa ggc ttc Asn Lys Pro Leu Phe Gln Ala Leu Ile Asp Gly Phe Arg Glu Gly Phe 325 330 335	1008
tat ttg ttt cct gat gga cga aat cag aat cct gat ctg act ggc tta Tyr Leu Phe Pro Asp Gly Arg Asn Gln Asn Pro Asp Leu Thr Gly Leu 340 345 350	1056

tgt gaa cca act ccc caa gac cat atc aaa gtg acc cag gaa caa tat 1104
 Cys Glu Pro Thr Pro Gln Asp His Ile Lys Val Thr Gln Glu Gln Tyr
 355 360 365

gaa tta tac tgt gag atg ggc tcc aca ttc caa cta tgt aaa ata tgt 1152
 Glu Leu Tyr Cys Glu Met Gly Ser Thr Phe Gln Leu Cys Lys Ile Cys
 370 375 380

gct gaa aat gat aag gat gta aag att gag ccc tgt gga cac ctc atg 1200
 Ala Glu Asn Asp Lys Asp Val Lys Ile Glu Pro Cys Gly His Leu Met
 385 390 395 400

tgc aca tcc tgt ctt aca tcc tgg cag gaa tca gaa ggt cag ggc tgt 1248
 Cys Thr Ser Cys Leu Thr Ser Trp Gln Glu Ser Glu Gly Gln Gly Cys
 405 410 415

cct ttc tgc cga tgt gaa att aaa ggt act gaa ccc atc gtg gta gat 1296
 Pro Phe Cys Arg Cys Glu Ile Lys Gly Thr Glu Pro Ile Val Val Asp
 420 425 430

ccg ttt gat cct aga ggg agt ggc agc ctg ttg agg caa gga gca gag 1344
 Pro Phe Asp Pro Arg Gly Ser Gly Ser Leu Leu Arg Gln Gly Ala Glu
 435 440 445

gga gct ccc tcc cca aat tat gat gat gat gat gat gaa cga gct gat 1392
 Gly Ala Pro Ser Pro Asn Tyr Asp Asp Asp Asp Asp Glu Arg Ala Asp
 450 455 460

gat act ctc ttc atg atg aag gaa ttg gct ggt gcc aag gtg gaa cgg 1440
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tag 1443

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<211> 480

<212> PRT

<213> c-Cbl480

<400> 262

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Phe Gln Pro His His His His His His His Leu Ser Pro His Pro Pro
 35 40 45

Gly Thr Val Asp Lys Lys Met Val Glu Lys Cys Trp Lys Leu Met Asp
 50 55 60

Lys Val Val Arg Leu Cys Gln Asn Pro Lys Leu Ala Leu Lys Asn Ser
 65 70 75 80

Pro Pro Tyr Ile Leu Asp Leu Leu Pro Asp Thr Tyr Gln His Leu Arg
 85 90 95

Thr Ile Leu Ser Arg Tyr Glu Gly Lys Met Glu Thr Leu Gly Glu Asn
 100 105 110

Glu Tyr Phe Arg Val Phe Met Glu Asn Leu Met Lys Lys Thr Lys Gln
 115 120 125

Thr Ile Ser Leu Phe Lys Glu Gly Lys Glu Arg Met Tyr Glu Glu Asn
 130 135 140

Ser Gln Pro Arg Arg Asn Leu Thr Lys Leu Ser Leu Ile Phe Ser His
 145 150 155 160

Met Leu Ala Glu Leu Lys Gly Ile Phe Pro Ser Gly Leu Phe Gln Gly
 165 170 175

Asp Thr Phe Arg Ile Thr Lys Ala Asp Ala Ala Glu Phe Trp Arg Lys
 180 185 190

Ala Phe Gly Glu Lys Thr Ile Val Pro Trp Lys Ser Phe Arg Gln Ala
 195 200 205

Leu His Glu Val His Pro Ile Ser Ser Gly Leu Glu Ala Met Ala Leu
 210 215 220

Lys Ser Thr Ile Asp Leu Thr Cys Asn Asp Tyr Ile Ser Val Phe Glu
 225 230 235 240

Phe Asp Ile Phe Thr Arg Leu Phe Gln Pro Trp Ser Ser Leu Leu Arg
 245 250 255

Asn Trp Asn Ser Leu Ala Val Thr His Pro Gly Tyr Met Ala Phe Leu
 260 265 270

Thr Tyr Asp Glu Val Lys Ala Arg Leu Gln Lys Phe Ile His Lys Pro
 275 280 285

Gly Ser Tyr Ile Phe Arg Leu Ser Cys Thr Arg Leu Gly Gln Trp Ala
 290 295 300

Ile Gly Tyr Val Thr Ala Asp Gly Asn Ile Leu Gln Thr Ile Pro His
 305 310 315 320

Asn Lys Pro Leu Phe Gln Ala Leu Ile Asp Gly Phe Arg Glu Gly Phe
 325 330 335

Tyr Leu Phe Pro Asp Gly Arg Asn Gln Asn Pro Asp Leu Thr Gly Leu
 340 345 350

Cys Glu Pro Thr Pro Gln Asp His Ile Lys Val Thr Gln Glu Gln Tyr
355 360 365

Glu Leu Tyr Cys Glu Met Gly Ser Thr Phe Gln Leu Cys Lys Ile Cys
370 375 380

Ala Glu Asn Asp Lys Asp Val Lys Ile Glu Pro Cys Gly His Leu Met
385 390 395 400

Cys Thr Ser Cys Leu Thr Ser Trp Gln Glu Ser Glu Gly Gln Gly Cys
405 410 415

Pro Phe Cys Arg Cys Glu Ile Lys Gly Thr Glu Pro Ile Val Val Asp
420 425 430

Pro Phe Asp Pro Arg Gly Ser Gly Ser Leu Leu Arg Gln Gly Ala Glu
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Gly Ala Pro Ser Pro Asn Tyr Asp Asp Asp Asp Asp Glu Arg Ala Asp
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<211> 2721

<212> DNA

<213> human c-Cbl wild type ORF

<400> 263

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caccacctca gccccaccc gccggggagc gtggacaaga agatgggtga gaagtgtctg	180
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ccaccttata tcttagacct gctaccagat acctaccagc atctccgtac tatcttgtca	300
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aatttgatga agaaaactaa gcaaacata agcctcttca aggagggaaa agaaagaatg	420
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ccttgaaga gctttcgaca ggctctacat gaagtgcac ccatcagttc tgggctggag	660
gccatggctc tgaaatccac tattgatctg acctgcaatg attatatttc ggtttttgaa	720

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ctccagaaat tcattcacaa acctggcagt tatactctcc ggctgagctg tactcgtctg	900
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tgtgaaatta aaggctactga acccatcgtg gtagatccgt ttgatcctag agggagtggc	1320
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